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Bioterrorism Agent Fact Sheet

Tularemia/*Francisella tularensis*

Disease

Tularemia is an uncommon zoonotic disease caused by the aerobic gram-negative bacilli, Francisella tularensis, and is endemic to North America and Eurasia. The natural cycle involves a mammal or tick host, but an intentional release would most likely be in the form of an aerosolization. Transmission occurs via bites from infected animals or insects, ingestion of infectious materials or inhalation of contaminated aerosols. Naturally occurring tularemia cases in Eurasia peak during summer months, while in North America the seasonal peak occurs in the spring and summer months. There are six forms of tularemia:

- Ulceroglandular tularemia (includes glandular, oculoglandular, and oropharyngeal):
  Make up over 45-85% (75-85%) of cases; mortality rate: < 2% (5%,4%) in untreated cases

- Septic tularemia **(not mentioned in Blue Book; some of the references lumped this together with typhoidal)**:
  Make up <5% of cases; mortality rate: 30-60%

- Pneumonic tularemia:
  Make up <5% of cases; mortality rate: 40-60% if untreated

  May be secondary to other form of tularemia (typically typhoidal or ulceroglandular) or be a primary infection following inhalation of infected particles.

- Typhoidal tularemia:
  Make up about 25% (5-15%) of cases; mortality rate: 35% in untreated cases or 1-3% in treated patients

  Most likely form if used as a bioweapon

Diagnosis

Presumptive diagnosis should be made on the basis of clinical findings and in conjunction with exposure information. A high level of suspicion is necessary; symptoms often resemble other infectious diseases including TB, plague, histoplasmosis, SEB and typhoid fever.

Definitive diagnosis may be made through culture isolation of F. tularensis or established retrospectively by serologic testing such as ELISA or bacterial agglutination. Clinical suspicion is essential because tularemia does not grow on standard culture media; cysteine- or sulfhydryl-enriched media must be specifically ordered when tularemia is suspected. Antibodies may be detected long after infection has resolved; titers should always be evaluated and only a = 4-fold increase considered to be an active infection. Specimens other than blood should be evaluated using direct fluorescent antibody testing.

Tularemia

Clinical Features of Tularemia

Early symptoms appear between 2-5 days (3-6 days) (range: 1-21 days) post exposure and manifest as sudden onset of flu-like symptoms: fever, chills, headache, cough, elevated WBC's and generalized body aches. Common elevated labs include lactic dehydrogenase, serum transaminases, and alkaline phosphatase; less common are elevations in serum creatine and myoglobin levels which could indicate rhabdomyolysis. Hematocrit, hemoglobin, platelets, and CSF are usually within normal ranges. Pneumonia may develop in any form of tularemia, but occurs in typhoidal tularemia most frequently (>80% of cases). Additional symptoms vary depending on the patients' form of tularemia:

Ulceroglandular tularemia:
Within days of exposure, over 85% of patients exhibit localized lymphadenopathy (> 1 cm in diameter) and 60% develop a localized cutaneous papule lesion (0.4 - 3.0 cm in diameter); the lesion progresses to a pustule and then ulcerates within a few days of its appearance. Approximately 30% of patients present with pneumonia.

Typhoidal tularemia:
Presents as a flu-like illness with fever, headache, generalized body aches, productive or non-productive cough, and infrequently, pleuritic pain or weight-loss. CXR may show pleural effusion (15% of patients) 2 or more commonly, evidence of pneumonia (80% of patients). This is the only form of tularemia that is not accompanied by lymphadenopathy.

Pneumonic tularemia:
Primary pneumonic tularemia presents as a flu-like illness with symptoms of upper respiratory infection with or without bronchopneumonia. Patients with secondary pneumonic tularemia exhibit similar flu symptoms in conjunction with

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Treatment

Treatment should begin as soon as diagnosis is suspected; early antibiotic therapy is highly effective. Streptomycin (0.5 g q12hrs IM X 7-10 days) has historically been the drug of choice (Streptomycin 7.5 - 10 mg/kg IM q 12hrs X 10-14 days; Streptomycin 30 mg/kg IM in 2 divided doses X 10-14 days); however, large quantities are not available. During an intentional release, Gentamycin should be utilized first. Penicillins and cephalosporins are not effective.

Gentamycin 3-5 mg/kg/day IV in equal divided doses q 8 hrs X 10 days (no mention of dividing the dose in Blue Book or Franz et al.: "3-5 mg/kg/day IV X 10 days") (Medical Letter: "1.5 mg/kg q 8 hrs IM X 10-14 days")

Alternatives:
Ciprofloxacin 400 mg IV q 12 hrs, switching to oral (500 mg q 12hrs) after clinical improvement; treatment should last at least 10 -14 days total.
Tetracycline or Chloramphenicol may be substituted, but should be given > 10 days to prevent relapses

Post-Exposure Prophylaxis

Limited studies indicate that 2-week courses of antibiotics administered within 24 hours of aerosol exposure are effective in preventing disease, but this is contraindicated for natural animal exposures:

Ciprofloxacin 500 mg PO q 12 hrs X 2 wks
Doxycycline 100 mg PO q 12 hrs X 2 wks
Tetracycline 500 mg PO q 6 hrs X 2 wks

Vaccination

A live-attentuated vaccine, live vaccine strain (LVS), is currently available as an FDA Investigational New Drug, but remains unavailable to the general public until further studies have been conducted. The vaccine is available for high risk laboratory workers and is administered by scarification. A live, attenuated vaccine is available in the US, but is limited to laboratory personnel who work with tularemia; effectiveness against aerosolized tularemia is not known. There is no vaccine available for the general public.

Additional information and references available at www.bioterrorism.slu.edu

signs of pneumonia, including bilateral lower lobe infiltrates and pleural effusions. Early symptoms of both include non-productive cough, pleuritic pain, dyspnea, and rarely, hemoptysis.

Infection Control

Only Standard precautions are necessary; person-to-person transmission has not been documented. Draining lesions should be covered following Standard precautions. F. tularensis is easily aerosolized in lab settings and is the cause of numerous documented lab-acquired infections. Because of this, many labs do not provide tularemia testing; labs that provide this service require biosafety level 2 precautions (level 3 precautions).

Decontamination

Tularemia can survive for weeks in water, soil and animal carcasses and is resistant to freezing temperatures, but is easily eradicated on surfaces by heat (55o C X 10 minutes) or standard hospital approved disinfectants.

Reporting

Report suspected cases or suspected intentional release of tularemia to your local health department. The local health department is responsible for notifying the state health department, FBI, and local law enforcement. The state health department will notify the CDC.

Disclaimer

Information contained in this fact sheet was current as of August 2001, and was designed for educational purposes only. Medication information should always be researched and verified before initiation of patient treatment.

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